

# **Exhibit 1**

# ORGANOGENESIS INC

## FORM 10-K (Annual Report)

Filed 3/31/1999 For Period Ending 12/31/1998

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Industry	Biotechnology & Drugs
Sector	Healthcare
Fiscal Year	12/31

**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549  
**FORM 10-K**

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d)  
OF THE SECURITIES EXCHANGE ACT OF 1934  
For the fiscal year ended December 31, 1998

*Commission File Number 1-9898*

**ORGANOGENESIS INC.**  
(Exact name of registrant as specified in its charter)

DELAWARE  
(State or other jurisdiction of  
incorporation or organization)

04-2871690  
(I.R.S. Employer  
Identification No.)

**150 DAN ROAD, CANTON, MA 02021**  
(Address of principal executive offices) (Zip Code)

**REGISTRANT'S TELEPHONE NUMBER, INCLUDING AREA CODE: (781) 575-0775**

**SECURITIES REGISTERED PURSUANT TO SECTION 12(B) OF THE ACT:**

Title of Each Class -----	Name of Each Exchange on Which Registered -----
Common Stock, \$.01 value	American Stock Exchange

**SECURITIES REGISTERED PURSUANT TO SECTION 12(G) OF THE ACT: NONE**

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ( ☒ ) No ( ☐ )

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ( ☐ )

The approximate aggregate market value of voting stock held by non-affiliates of the registrant was \$397,799,079 based on the last reported sale price of the company's common stock on the American Stock Exchange as the close of business on March 4, 1999. There were 30,453,518 shares of common stock outstanding as of March 4, 1999, excluding treasury shares.

**DOCUMENTS INCORPORATED BY REFERENCE**

Document -----	Part of Form 10-K into which incorporated -----
Portions of the Registrant's Definitive Proxy Statement for its 1999 Annual Meeting of Stockholders.....	III

With the exception of the portions of the Definitive Proxy Statement for the registrant's 1999 Annual Meeting of Stockholders expressly incorporated into this Report by reference, such document shall not be deemed filed as a part of this Annual Report on Form 10-K.

**PART I**

This Form 10-K contains forward-looking statements that involve risks and uncertainties. Forward-looking statements include information on:

- . Our business outlook and future financial performance;
- . Anticipated profitability, revenues, expenses and capital expenditures;
- . Future funding and expectations as to any future events; and
- . Other statements that are not historical fact and are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that involve risks and uncertainties.

Although we believe that our plans, intentions and expectations reflected in or suggested by such forward-looking statements are reasonable, we can give no assurance that such plans, intentions or expectations will be achieved. When considering such forward-looking statements, you should keep in mind the risk factors and other cautionary statements in this Form 10-K. The risk and other factors noted throughout this Form 10-K could cause our actual results to differ materially from the results contained in any forward-looking statements.

**ITEM 1. BUSINESS**

Organogenesis Inc. designs, develops and manufactures medical therapeutics containing living cells and/or natural connective tissue. The company was formed to advance and apply the emerging field of tissue engineering to major medical needs. Our lead product, Apligraf(R), was launched in the US - the world's largest healthcare market - in June 1998. Apligraf is the only mass- manufactured product containing living human cells to show efficacy in a controlled study and gain FDA PMA approval. Organogenesis was organized as a Delaware corporation in 1985, with principal offices located at 150 Dan Road, Canton, Massachusetts 02021. The telephone number is 781/575-0775.

Tissue engineering and product development - We have an FDA-inspected, GMP- compliant facility. We have experience manufacturing living, cellular products and make Apligraf for commercial sale. Tissue-engineered products typically include living cells and/or natural connective tissue material such as collagen. We have established expertise with both mammalian (e.g., human) cells and natural connective tissue and select our product development approach based on medical application. Our pipeline includes both cellular and acellular programs.

Commercialization strategy - Our strategy is to commercialize products either by ourselves or through partners with an established marketing presence. For example, Novartis Pharma AG has global marketing rights to Apligraf and is responsible for sales and marketing costs (see "Collaborative and Other Agreements"). We have an active business development program related to products and technologies in our pipeline.

**PRODUCTS**

Our product development program includes living tissue replacements, cell- based organ assist devices and other tissue-engineered products. The following table shows products/research programs in our pipeline, potential uses and current status.

Apligraf(R) is a registered trademark of Novartis.

PRODUCT	POTENTIAL INDICATION/USE	STATUS
=====		
CELLULAR:		
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Apligraf	Venous leg ulcers	Pivotal trial completed and published; approved and marketed in US and Canada
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Apligraf	Diabetic foot ulcers	Patient enrollment completed in pivotal trial; trial to complete 5/99
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Apligraf	Burns	Study completed
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Apligraf	Skin surgery	Studies completed in dermatologic surgery and in donor site wounds; cosmetic outcome pivotal trial underway in dermatologic surgery
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Apligraf	Epidermolysis bullosa	Study underway through physician IDE
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Apligraf	Pressure sores	Study planned
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Vitrix(TM)	Dermal replacement, plastic/reconstructive surgery, oral surgery	Expected to enter pilot trials in 1999
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Bioartificial liver	Bridge-to-transplant, chronic liver disease	Research & development
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Cell therapies	Diabetes	Research & development
-----		
ACELLULAR:		
=====		
GraftPatch(TM)	Soft tissue reinforcement (e.g., hernia repair)	Cleared for marketing in US
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Engineered collagen fibrils	Tissue scaffold applications	Research & development
-----		
Vascular graft	Peripheral and coronary bypass	Research & development
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Organogenesis also began selling TestSkin II, an in vitro testing product in December 1998.

**APLIGRAF**

Product Description - Our most advanced product is Apligraf living skin construct. Like human skin, Apligraf is living, all natural and bi-layered, with both an upper epidermal and a lower dermal layer. It contains living human skin cells - epidermal keratinocytes and dermal fibroblasts. The keratinocytes are differentiated to form the strata of the human epidermis, including the outer stratum corneum. Unlike human skin, Apligraf does not contain structures such as blood vessels, hair follicles and sweat glands.

[Photo showing structure of Apligraf compared to Human Skin]

Under the microscope, as shown above, Apligraf shares the appearance of skin.

Commercialization - Apligraf was approved for marketing by the US FDA on May 22, 1998. It is approved for the treatment of venous leg ulcers. Additional potential uses include the treatment of other chronic wounds (e.g., diabetic ulcers, pressure sores) as well as acute wounds (e.g., skin surgery, burns). Novartis Pharmaceuticals Corporation markets Apligraf in the US. Novartis also markets the product in Canada, with launches expected in Europe in 1999. Novartis' initial marketing strategy is to establish Apligraf as the new standard of care for venous leg ulcers.

**Current and Potential Markets -**

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CURRENT AND POTENTIAL APLIGRAF MARKETS	
=====	
INDICATION	APPROXIMATE # OF
-----	PATIENTS/PROCEDURES
CHRONIC WOUNDS:	-----
Venous leg ulcers	1,000,000 patients
Diabetic ulcers	600,000 patients
Pressure sores	2,000,000+ patients
SKIN SURGERY WOUNDS	600,000 procedures per year
SEVERE BURNS WOUNDS	12,000 procedures per year
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Venous leg ulcers: Apligraf is approved for marketing in the US for the treatment of venous leg ulcers of greater than one month duration that have not responded to conventional therapy. Approximately one million people in the US suffer from venous leg ulcers. Over half of these patients have hard-to-heal wounds, such as long-standing ulcers, testament to the need for more effective therapies. In its pivotal trial, Apligraf was shown to heal more patients, faster, than standard care alone. Apligraf can also be cost effective: at the current US pricing of approximately \$975 per unit, Apligraf can be the most cost-effective option for many venous leg ulcer patients. Apligraf is currently being reimbursed in the US on a case-by-case basis. Novartis is working to gain standardized reimbursement.

Diabetic foot ulcers: In 1998, patient enrollment was completed in the diabetic foot ulcer pivotal trial, making Apligraf the most advanced living product in development for the treatment of diabetic ulcers in the US. Approximately 600,000 people in the US suffer from diabetic ulcers. A major medical need, these ulcers can frequently lead to amputation: 50,000 - 60,000 amputations occur among diabetics in the US each year.

The diabetic ulcer study is a large, prospective, randomized, controlled multi-center trial comparing Apligraf with current standard care for diabetic foot ulcers. Twenty-four centers across the US are participating in the study, including nationally-renowned diabetes treatment centers. The study includes over 200 patients and is expected to yield a number of publications and presentations beginning in 1999.

Other potential opportunities: Other potential uses for Apligraf include skin surgery and burns. Apligraf studies have been completed in dermatologic surgery, donor site wounds and in severe burns, with publications from each expected to be available in 1999. For example, in February 1999, data from the Apligraf study in burns were presented at the John A. Boswick, MD, Burn & Wound Care Symposium.

Traditional wound studies have often focused on frequency and time to healing without regard to scarring. Based on information from previous studies, including the burn trial, in 1998 we initiated a prospective, multi-center study specifically to assess the cosmetic outcome of wounds healed with Apligraf versus standard care. This study is being conducted in wounds due to skin cancer removal, as these typically occur in cosmetically-important areas of the body.

A widening body of clinical data on Apligraf is expected to become available as, now that the product is on the market, individual physicians and Novartis can conduct and publish their own studies. We expect to add to this body of information with a study in pressure sores planned to begin in 1999.

We have the ability to cryopreserve or "freeze" Apligraf. Cryopreserved Apligraf can be stored essentially indefinitely while maintaining greater than 90% cell viability. In addition to the potential opportunities this provides with Apligraf, we expect that our unique, patent-protected cryopreservation technology could be beneficial in the development of our other cellular products.

With Apligraf, we have demonstrated our ability to tap the power of living cells and natural connective tissue. We are applying this expertise to the development of other potentially important products.

#### **VITRIX**

Vitrix is a soft tissue replacement product comprised of natural collagen and living human fibroblasts, two components of Apligraf. We plan to initiate pilot clinical trials with Vitrix in 1999.

The impetus for Vitrix development was the medical need for a non-inflammatory product that could replace soft tissue lost or damaged through surgery, deep wounds or other injury. Examples of potential Vitrix applications include as a dermal replacement, for tissue bulking in various applications in plastic/reconstructive and general surgery and for mucosal tissue repair (e.g., periodontal procedures).

The profile of Vitrix leverages information and processes we have already established with Apligraf. For example, all components in Vitrix are included in Apligraf. Thus, Vitrix uses component sourcing processes and safety information we have already established with Apligraf. Similarly, synergies in Vitrix manufacturing leverage Apligraf production processes and equipment.

These synergies are expected to help reduce the cost of the Vitrix program, as well as advance Vitrix development faster, and at lower risk, than typical for many new medical products. We hold both marketing and manufacturing rights to Vitrix, providing options for commercialization strategies.

### **BIOARTIFICIAL LIVER**

Each year in the US, approximately 250,000 people are hospitalized with liver insufficiency and 45,000 people die from liver failure. Currently, transplantation is the only effective means of treating liver failure. However, it is not an option for many patients, and, among the severely ill patients who do receive a liver, one in four requires a second transplant due to deteriorated health. Ironically, the liver is a highly regenerative organ. Some patients would not need a transplant if there were a simpler way to receive liver function until their own organ recovered.

We are developing a bioartificial liver - an extracorporeal device - to provide liver function until the patient recovers or receives a liver transplant. We believe the key to an effective bioartificial liver is providing healthy, highly functional liver cells. Thus, this program leverages our proven expertise in cell procurement, culture and optimization. We have augmented our internal team with additional experts in bioartificial device design. We also have a research collaboration with the Massachusetts General Hospital to access their knowledge of bioartificial liver device design. We expect to collaborate with multiple medical institutions as the program progresses through design, development and testing stages.

Our achievements to date include: defining the method for effective liver cell isolation; evaluation of liver cell culture procedures to achieve desired functionality; development of innovative device designs; and establishment of a small animal model of liver failure in which prototype device designs are being tested.

While a significant scientific challenge, potential benefits of our bioartificial liver program are expected to include reducing mortality among patients awaiting a liver, improving the success rate of first transplants, reducing the overall need for liver transplantation and assisting patients not currently qualifying for transplantation.

### **OTHER CELLULAR PROGRAMS**

We continue to leverage our cellular expertise to further expand and strengthen our pipeline. Examples include:

- . In December 1998, we began selling TestSkin II, a skin-like in vitro testing product for use by pharmaceutical, cosmetic, drug delivery and academic scientists and quality control professionals in product development and testing.

- . We have an early stage research program related to cell therapies, including culturing of islet cells, for the treatment of diabetes.

## VASCULAR GRAFT

Nearly 300,000 coronary artery bypass procedures are performed in the US alone each year. Each of these bypass procedures requires an average of 3.5 grafts. Surgeons still rely on vein harvested from the patient for graft material. This is because patient vein provides a feature that has proven unobtainable with synthetics: the ability to provide critical strength while becoming populated with patient cells, thus maintaining short-term and long-term blood flow. Use of patient vein, however, has its drawbacks. The patient may not have sufficient healthy vein available for the grafts needed. Harvesting vein can greatly extend the duration and thus the cost of the procedure. It also creates a second wound site, increasing patient discomfort and the risk of complications.

We are developing a vascular graft intended to provide the performance of patient vein with the advantage of being off-the-shelf. The graft, currently in animal studies, is designed to provide the necessary physical strength of a blood vessel while becoming converted into living tissue through inward migration of the patient's own cells. Studies done in a small animal model show that our vascular graft, implanted as an acellular collagen tube, is remodeled in the body into cellularized, living tissue.

## OTHER ACELLULAR PROGRAMS

Our research programs have spawned two additional potential licensing opportunities - GraftPatch and engineered collagen fibrils.

**GraftPatch** - GraftPatch is cleared for marketing for soft tissue reinforcement (e.g., hernia repair) through the FDA 510k process. Preclinical studies have indicated that GraftPatch provides mechanical strength while avoiding the formation of post-surgical adhesions. To maintain our research and manufacturing focus on more significant product opportunities, we intend to out-license GraftPatch.

**Engineered Collagen Fibrils** - Collagen injections are used to provide local tissue bulking to, for example, treat female urinary incontinence and soften wrinkles. Available products have been found to disperse after injection, limiting long-term benefit. We have proprietary technology to produce collagen fibrils or "strings". These fibrils are short enough to fit through a needle, yet long enough to intertangle and provide bulk post-injection. This technology is also considered to be a potential out-licensing opportunity. To maintain our research and manufacturing focus on more significant product opportunities, we intend to out-license our engineered collagen fibrils for tissue bulking purposes.

## RISK FACTORS

### **Our Markets Are Competitive**

We are engaged in the rapidly evolving and competitive field of tissue engineering for the treatment of skin wounds and other medical needs. Our competitors include tissue engineering companies, xenotransplant companies, wound care divisions of major pharmaceutical companies and other pharmaceutical, biotechnology and medical products companies using traditional technologies to develop products for wound care. Some of these companies have much greater resources, research and development staffs and facilities, experience in conducting clinical trials and obtaining regulatory approvals and experience in the manufacturing, marketing and distribution of products than we do. Our competitive position is based upon our ability to (1) create and maintain scientifically-advanced technology and proprietary products and processes, (2) attract and retain qualified personnel, (3) obtain patent or other protection for our products and processes, (4) obtain required government approvals on a timely basis, (5) manufacture products on a cost-effective basis and (6) successfully market products. If we are not successful in meeting these goals, our business could be hurt. Similarly, our competitors may succeed in developing technologies, products or procedures that are more effective than any that we are developing or that would render our technology and products obsolete, noncompetitive or uneconomical.

### **The Retention of Key Personnel Is Important to Our Competitive Position**

Because of the specialized nature of our business, our success will depend upon our ability to attract and retain highly-qualified personnel and to develop and maintain relationships with leading research institutions. The competition for those relationships and for experienced personnel amongst the biotechnology, pharmaceutical and healthcare companies, universities and non-profit research institutions is intense. If we are unable to continue to attract and retain such personnel or relationships, our competitive position could be hurt.

### **We Rely Heavily Upon Our Patents and Proprietary Technology**

We rely upon our portfolio of patent rights, patent applications and exclusive licenses to patents and patent applications relating to living tissue products, organ assist treatments and other aspects of tissue engineering. We currently have twenty patents issued or allowed in the US, nine pan-European patents issued and six patents issued in Japan. As part of our continuing interest in protecting intellectual property rights, we have filed and are prosecuting fourteen other patent applications in the US. We also license some of our technologies under an exclusive patent license agreement with the Massachusetts Institute of Technology. The agreement with MIT covers certain US patents and corresponding patents in European and Far East countries. Pursuant to the MIT agreement, we have been granted an exclusive, worldwide license to make, use and sell the products covered by the patents and to practice the procedures covered by the patents.

We expect to aggressively patent and protect our proprietary technologies. However, we cannot be sure that any additional patents will be issued to us as a result of our domestic or foreign patent applications or that any of our patents will withstand challenges by others. Patents issued to or licensed by us may be infringed or third parties may independently develop either the same or similar technology. Similarly, our patents may not provide us with meaningful protection from competitors, including those who may pursue patents which may prevent, limit or interfere with our products or will require licensing and the payment of significant fees or royalties by us to such third parties in order to enable us to conduct our business. We may sue or be sued by third parties regarding patents and other intellectual property rights. These suits are costly and would divert funds and management and technical resources from our operations.

We also rely upon unpatented proprietary technology, know-how and trade secrets and seek to protect them through confidentiality agreements with employees, consultants and advisors. We request that any corporate sponsor with which we enter into a collaborative agreement do so as well. If these confidentiality agreements are breached, we may not have adequate remedies for the breach. In addition, others may independently develop or otherwise acquire substantially the same proprietary technology as our technology and trade secrets.

We have relationships with a number of academic consultants who are not employed by us. Accordingly, we have limited control over their activities and can expect only limited amounts of their time to be dedicated to our activities. These persons may have consulting, employment or advisory arrangements with other entities that may conflict with or compete with their obligations to us. Our consultants typically sign agreements that provide for confidentiality of our proprietary information and results of studies. However, in connection with every relationship, we may not be able to maintain the confidentiality of our technology, the dissemination of which could hurt our competitive position and results of operations. To the extent that our scientific consultants develop inventions or processes independently that may be applicable to our proposed products, disputes may arise as to the ownership of the proprietary rights to such information, and we may not win those disputes.

#### Our Ability to Commercialize Our Products Depends Upon Our Compliance with Government Regulations

Our present and proposed activities are subject to extensive and rigorous regulation by governmental authorities in the US and other countries. To clinically test, produce and market medical devices for human use, we must satisfy mandatory procedural and safety and efficacy requirements established by the FDA and comparable state and foreign regulatory agencies. Typically, such rules require that products be approved by the government agency as safe and effective for their intended use prior to being marketed. The approval process is expensive, time consuming and subject to unanticipated delays. Our product candidates may not be approved. In addition, our product approvals could be withdrawn for failure to comply with regulatory standards or due to unforeseen problems after the product's marketing approval.

Testing is necessary to determine safety and efficacy before a submission may be filed with the FDA to obtain authorization to market regulated products. In addition, the FDA imposes various requirements on manufacturers and sellers of products under its jurisdiction, such as labeling, Good Manufacturing Practices, record keeping and reporting requirements. The FDA also may require post-marketing testing and surveillance programs to monitor a product's effects. Furthermore, changes in existing regulations or the adoption of new regulations could prevent us from obtaining, or affect the timing of, future regulatory approvals or could negatively affect the marketing of our existing products. If

(1) the regulatory agencies find our testing protocols to be inadequate, (2) the appropriate authorizations are not granted on a timely basis, or at all, (3) the process to obtain authorization takes longer than expected or we have insufficient funds to pursue such approvals, (4) we lose previously-received authorizations or (5) we do not comply with regulatory requirements, we would not be able to commercialize our products as planned and our operating results would be hurt.

Medical and biopharmaceutical research and development involves the controlled use of hazardous materials, such as radioactive compounds and chemical solvents. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of such materials and waste products. In addition, we handle and dispose of human tissue. Although we believe that our safety procedures for handling these materials are adequate, if accidental contamination or injury were to occur, we could be liable for damages.

#### We May Be Subject to Product Liability Suits; Our Insurance May Not Be Sufficient to Cover Damages

Our business exposes us to potential liability risks that are inherent in the testing, manufacturing, marketing and sale of medical products. The use of our products and product candidates, whether for clinical trials or commercial sale, may expose us to product liability claims or product recall and possible adverse publicity. Although we have product liability insurance coverage, the level or breadth of our coverage may not be adequate to fully cover potential liability claims. In addition, we may not be able to obtain additional product liability coverage in the future at an acceptable cost. A successful claim or series of claims brought against us in excess of our insurance coverage, and the effect of product liability litigation upon the reputation and marketability of our technology and products, together with the diversion of the attention of key personnel, could negatively affect our business.

#### We Must Be Able to Manufacture Our Products Successfully and Obtain Adequate Sources of Supply

The process of manufacturing our products is complex, requiring strict adherence to manufacturing protocols. We have been producing our lead product, Apligraf, for commercial

sale since the second half of 1997 in adherence with these manufacturing protocols. However, with increasing demand for Apligraf, we must further transition from small-scale to full-scale production of our products. If we do not make the full transition successfully, we will not be able to satisfy the demands for our products and our results of operations will be hurt.

We are required to maintain a manufacturing facility in compliance with Good Manufacturing Practices. Manufacturing facilities and processes pass an inspection before the FDA issues any product licenses necessary to market medical therapeutics and are subject to continual review and periodic inspection. We may not be able to maintain the necessary regulatory approvals for our manufacturing operations or manufacture our products in a cost-effective manner. If we were unable to manufacture potential products independently or obtain or retain third party manufacturing on commercially-acceptable terms, the submission of products for final regulatory approval and initiation of marketing would be delayed. This, in turn, may cause us to be unable to commercialize product candidates as planned, on a timely basis or on a profitable basis.

We manufacture Apligraf for commercial sale, as well as for use in clinical trials, at our Canton, Massachusetts facility. Among the fundamental raw materials needed to manufacture Apligraf are keratinocyte and fibroblast cells. Because these cells are derived from donated infant foreskin, they may contain human-borne pathogens. We perform extensive testing of the cells for pathogens, including the HIV or "AIDS" virus. Our inability to obtain cells of adequate purity, or cells that are pathogen-free, would limit our ability to manufacture sufficient quantities of our products.

Another major material required to produce our products is collagen, a protein obtained from animal source tissue. We have developed a proprietary method of procuring our own collagen that we believe is superior in quality and strength to collagen available from commercial sources. We currently obtain animal source tissue from US suppliers only. We may not be able to obtain adequate supplies of animal source tissue to meet our future needs or on a cost-effective basis. The thermo-formed tray assembly that is used in the manufacturing process of Apligraf is available to us under a supply arrangement with only one manufacturing source. Because the FDA approval process requires manufacturers to specify their proposed materials of certain components in their applications, FDA approval of a new material would be required if a currently-approved material became unavailable from a supplier. If we are unable to obtain adequate supplies of thermo-formed tray assemblies to meet future Apligraf manufacturing needs or if we cannot obtain such assemblies on a cost-effective basis, our operations would be hurt. .

Interruptions in our supply of materials may occur in the future or we may have to obtain substitute vendors for these materials. Any significant supply interruption would adversely affect the production of Apligraf. In addition, an uncorrected impurity or a supplier's variation in a raw material, either unknown to us or incompatible with our manufacturing process, could hurt our ability to manufacture products.

Our Business Is Subject to the Uncertainty of Third-Party Reimbursement and Health Care Reform Measures Which May Limit Market Acceptance

In both domestic and foreign markets, our ability to commercialize our product candidates will depend, in part, on upon the availability of reimbursement from third-party payors, such as government health administration authorities, private health insurers and other organizations. Third-party payors are increasingly challenging the price and cost-effectiveness of medical products. If our products are not considered cost effective, third-party payors may limit reimbursement. Government and other third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement for new therapeutic products approved for marketing by the FDA and by refusing, in some cases, to provide any coverage for uses of approved products for disease indications for which the FDA has not granted marketing approval. If government and third-party payors do not provide adequate coverage and reimbursement levels for uses of our products, the market acceptance of our products would be limited.

There have been a number of federal and state proposals during the last few years to subject the pricing of pharmaceuticals to government control and to make other changes to the health care system of the US. It is uncertain what legislative proposals will be adopted or what actions federal, state or private payors for health care goods and services may take in response to any health care reform proposals or legislation. We cannot predict the effect health care reforms may have on our business.

#### **We Depend Upon Strategic Relationships to Market Our Products**

We have limited experience in sales, marketing and distribution. We will need to develop long-term strategic relationships with partners, such as Novartis, that have marketing and sales forces with technical expertise and distribution capability. To the extent that we enter into such relationships, our revenues will depend upon the efforts of third parties who may or may not be successful. We may not be able to establish or maintain long-term strategic relationships, and if we do, our collaborators may not be successful in gaining market acceptance for our products. To the extent that we choose not to or are unable to negotiate or maintain collaborations, we will need more capital and resources to undertake a commercialization program at our own expense. In addition, we may encounter significant delays in introducing our products into certain markets or find that the commercialization of products in such markets may be adversely affected by the absence of collaborative agreements. We are dependent on Novartis for the successful marketing and selling of Apligraf worldwide. If Novartis does not succeed in marketing and selling Apligraf or gaining international approvals for the product or if we are unable to meet the production demand of global commercialization, our operating results will suffer.